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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,391	07/07/2000	JEROEN KRIJGSVELD	702-000648	1936

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EXAMINER	
SNEDDEN, SHERIDAN	
ART UNIT	PAPER NUMBER

1653

DATE MAILED: 06/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/509,391	KRIJGSVELD ET AL.
	Examiner Sheridan K Snedden	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-21 is/are pending in the application.
 - 4a) Of the above claim(s) none is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-21 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>78</u> . | 6) <input type="checkbox"/> Other: _____. |

DETAILED ACTION

1. Claims 1-21 are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Since all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, the restriction requirement made in Paper No. 9 is hereby withdrawn.

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

3. The drawings filed on July 7, 2000 are acceptable subject to correction of the informalities indicated on the attached "Notice of Draftperson's Patent Drawing Review," PTO-948. In order to avoid abandonment of this application, correction is required in reply to the Office action.

The correction will not be held in abeyance.

Claim Objections

4. The claims are objected to for not complying with the sequence rules of 35 CFR 1.821(d), which states that a reference must be made to a sequence described to in the text of the description or claims by use of the sequence identifier, preceded by "SEQ ID NO:."

Specification

5. The specification is objected to for not complying with the sequence rules of 35 CFR 1.821(d), which states that a reference must be made to a sequence described to in the text of the

description or claims by use of the sequence identifier, preceded by "SEQ ID NO.: " (see specification page 2, lines 1 and 2, for example).

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 22 and objected claims thereto are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. As stated, the claims recite a peptide of natural origin and do not show the hand of man. Applicant is advised to include the words "isolated" or "purified" in the recitation of the invention directed towards protein to indicate the hand of man.

8. Claims 33-35 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 22 and dependent claims thereto are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 22 and dependent claims thereto are rejected because it is unclear as to which specific arrangement the claim refers.

11. Regarding claim 28 and 29, the phrase "for example" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

12. Claims 25 and 26 are rejected because the meaning of 'variant' is unclear. The term 'variant' is defined on page 2 of the specification as having at least 70% identity to TC-1 or TC-2. Claims 25 and 26 recite a sequence at least in part of TC-1 and TC-2. It is unclear as to which definition sets the limitation of the claim.

Claim Rejections - 35 USC § 102

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

14. Claims 22-27 are rejected under 35 U.S.C. 102(b) as being anticipated by Daly *et al.* (Patent No: 5,656,724). Daly *et al.* disclose recombinant (claim 27) CXC chemokines (claim 24) whose amino acid sequences, SEQ ID NO: 9 and 10, comprise the exact same amino acid sequence of TC-1, SEQ ID NO: 6, and TC-2, SEQ ID NO: 12 (claims 25 and 26). In addition,

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Daly *et al.*, column 1 line 32, disclose these CXC chemokines as small inducible proteins having a specific arrangement of four position-invariant cysteine residues in their primary amino acid sequence that form two disulfide bonds (claims 22 and 23).

15. Claims 22-29 and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Baggolini *et al.* (WO 90/06321). Baggolini *et al.* teach the administration of daily doses (claim 33) of recombinant CXC chemokine (claims 24 and 27) NAP-2 for the treatment of human conditions (claim 31) associated with bacterial and fungal infections (page 9 third paragraph) (claims 28 and 29). Comparison of the sequences given in figure 1 of the specification show that NAP-2 is 97% identical of TC-1 (SEQ ID NO: 6) and 82% identical TC-2 (SEQ ID NO: 12). This % meets the limitation of variants as defined on page 2 of the specification (claims 25 and 26). Additionally, as disclosed in the specification, the arrangement, disulfide linkages and 3-dimensional structure are inherent properties to this class of antimicrobial peptides (claims 22-23). Therefore, NAP-2 may be considered a variant of TC-1 and TC-2, and thus anticipates the invention.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

17. Claims 22, 32 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baggolini *et al.* (WO 90/06321) in view of Cimbollek *et al.* (1996). Baggolini *et al.* disclose

the antimicrobial NAP-2, a CXC chemokines a specific arrangement of four position-invariant cysteine residues in their primary amino acid sequence that form two disulfide bonds. Baggolini *et al.* does not disclose the CXC chemokines for the treatment of bacterial and fungal endocarditis.

Cimballek *et al.* teach that both fungal and bacterial infections are associated with endocarditis (page 1432, first paragraph).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the known antimicrobial chemokine, NAP-2, for the treatment of endocarditis caused by fungal and bacterial infection. The person of ordinary skill in the art would have been motivated to treat endocarditis with the above chemokine because the chemokine has known antimicrobial activity. The person of ordinary skill in the art would have expected success because endocarditis is caused by both fungal (claim 34) and bacterial (claim 32) infections (Cimballek *et al.*). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

18. Claims 22, 30 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baggolini *et al.* (WO 90/06321) in view of Pollock *et al.* (Patent No: 4,725,576) and in further view of Benson *et al.* (Patent No: 5,073,627). Baggolini *et al.* disclose the antimicrobial NAP-2, a CXC chemokines a specific arrangement of four position-invariant cysteine residues in their primary amino acid sequence that form two disulfide bonds. Baggolini *et al.* does not disclose the CXC chemokines as being fused with a Histag having enhanced antimicrobial activity.

Pollack *et al.* teaches that antimicrobial effects of L-histidine and histidine-rich polypeptides. Specifically, Pollack *et al.* teach the antimicrobial effects of His-7 and His-4,

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containing 4 and 7 residues of L-histidine, respectively (example IV). Additionally, Pollack *et al.* teaches that L-histidine and histidine-rich polypeptides have antimicrobial activity (see columns 3 and 4).

Benson *et al.* teach a fusion protein made by combining GM-CSF and IL-3. GM-CSF and IL-3 have considerable overlap in their range of biological activities. Example 4 of Benson *et al.* show that the fusion protein has enhanced biological activity when compared to IL-3 or GM-CSF alone.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to fuse a histag, or His-6, to the NAP-2, a known CXC chemokine having a specific arrangement and disulfide-linkage of 4 cysteine residue, in order to achieve enhanced activity. The person of ordinary skill in the art would have been motivated to add a histag to the known chemokines because both NAP-2 and L-Histidine have antimicrobial activity (Baggiolini *et al.* and Pollock *et al.*). The person of ordinary skill in the art would have expected success, because combining peptides with overlapping activities results in a fusion protein with enhanced activity (Benson *et al.*). Thus, the claimed invention was within the ordinary skill in the art to make and use at the time it was made and was as a whole, *prima facie* obvious.

Advisory Information

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (703) 305-4843. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-3975 for regular communications and (703) 746-3975 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
June 6, 2002

Karen Cochran Carlson, Ph.D.
KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER